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EXAMINER	
NASHED, NASHAAT T	

ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
02/22/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/518,072	WEILL ET AL.	
	Examiner	Art Unit	
	NASHAAT T. NASHED	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *9-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5 and 7* is/are rejected.

7)☒ Claim(s) *4,6 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/16/04* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/11/05 & 4/22/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election with traverse of Group I, claims 1-8 as they relate to SEQ ID NO:1 in the reply filed on November 2, 2009 is acknowledged. The traversal is on the ground(s) that examining and searching all claims would not require undue search burden. This is not found persuasive. First, the inventions lack unity of invention when the special technical feature of the invention is the contributed to the art by others. Based on the search report, acetylcholine esterase comprising catalytic region having 60% sequence homology to SEQ ID NO: 1 were known in the prior art. The search report list 12 X references against claims 1, 3, 5, and 8-11 which comprise claims to polypeptides and nucleic acid sequences. Also, see the rejection under 35 USC 102 (b)/103 below. The search burden is *prima facie* obvious in view of the number of the polypeptide and nucleic acid sequences to be searched. It should be noted that the nucleic acid sequences, polypeptide, and antibodies are distinct chemical compounds. While searching each of the chemical compounds may overlap, each of the claimed chemical entities requires its separate and independent searches in the patent and non-patent literature.

The requirement is still deemed proper and is therefore made FINAL.

Since searching SEQ ID NO: 1 produced sufficient result to examine SEQ ID NO: 3, 5, 7, 57, 122, and 126, the restrictions between these sequences are hereby vacated.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s). In particular, applicants' attentions are directed to 37 CFR 1.821, which states:

> (d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

For example, Figures 2, 5, 6A, 6B, 9A, 9B, 13 and 14 contain amino or nucleic acid sequences which are not accompanied by sequence identification numbers in the Figure or the Figure description. Perfecting the compliance with the sequence rule is required.

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because Figures 1, 2, 5, 6A and B, 9A and B, 13, and 14 are of low quality and hard to read and do not show clearly what is being described in the specification. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

The attempt to incorporate subject matter into this application by reference to NCBI sequence AAK0973 and SWISSPROT P04058 is ineffective because it constitute improper incorporation by reference. See for example pages 5, 7, 9, and 11 and claims 1, 2, and 4. The amino acid sequences of NCBI sequence AAK0973 and SWISSPROT P04058 are considered essential subject matter which can be incorporated by reference only by referencing U. S. patent or U. S. patent publication. The databases referenced are not U. S. patent or patent publication.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See for example page 7, line 5, page 23, line 8, page 31, lines 27, 29, and 36, and page 32, paragraphs 1 and 3. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claims 2-8 are objected to because of the following informalities: (a) The phrase "as claimed in" should be replace with ----of----, and (b) replace the phrase "chosen from" with ---selected from the group consisting of----. Appropriate correction is required.

Claims 4, 6, and 8 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from a multiple dependent claim. Claim 3 is a multiple dependent claim and multiple dependent claims 4, 6, and 8 are dependent on claim 3. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

35 U.S.C. 101 reads as follows:
"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1, 2, 3, 5 and 7 are rejected under 35 U.S.C. 101 because the claimed invention is directed toward non-statutory subject matter.

In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter. *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims to contain wording such as "An isolated and purified protein or nucleic acid".

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5, and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) The reference to a sequence in a database by accession number in claims 1 and 2 renders the claims indefinite because the resulting claim does not define the metes and bound of the desired patent protection. Since the referenced residue 119 could not be identified with any certainty, the limitation is disregarded in examination.

(b) The phrase "sequence similarity" in claim 1 renders the claim indefinite because the resulting claim does not define the metes and bound of the desired patent protection. It is noted that the phrase is defined in the specification at page 6, line 16-28. The definition, however, does not define the metes and bound in the phrase with any particularity. No penalties are assessed on gapes and insertion, or description of what is conservative substitution and what is not.

(c) The clause "it corresponds to that" in claim 3 renders the claim indefinite because the resulting claim does not set forth the metes and bound of the desired patent protection. The phrase is not defined by the claim and one of ordinary skill in the art would not know in what way the acetylcholinesterase corresponds to those from the listed genera. For examination purposes only, claim is interpreted to mean correspond to any acetylcholinesterase obtained from.

(d) Claim 5 is included in this rejection because it is dependent from rejected claims and does not cure their deficiencies.

> The following is a quotation of the first paragraph of 35 U.S.C. 112:
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5, and 7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. While the claims are enabled for insect acetylcholinesterase comprising an amino acid sequence having 90% sequence identity to SEQ ID NO: 1, the claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to the all possible insect cholinesterases comprising a catalytic region having 60% sequence identity or 70% sequence similarity to SEQ ID NO: 1. Factors to be considered in determining whether undue

experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any polypeptide sequence comprising an amino acid sequence having 60% sequence identity or 70% sequence similarity to SEQ ID NO:1 from any biological and man-made source. That include all possible insertion, deletion substitution and combination thereof mutants of up to 40% of the 524 amino acid residues of SEQ ID NO:1. The specification provides guidance and examples in the form of an assay to identify the nucleic acid sequences encoding the polypeptide and the polypeptide themselves of SEQ ID NO: 3, 5, 7, 57, 122, and 126 and identify the catalytic domain to be the amino acid sequence of SEQ ID NO: 1. (see examples). The catalytic domains of SEQ ID NO: 3, 5, and 126 are identical and identical to SEQ ID NO:1. Also, the catalytic domains of SEQ ID NO's: 122, 7, and 57 are 99.8%, 94.3%, and 94.1% identical to SEQ ID NO:1, respectively. While molecular biological techniques and genetic manipulation to make any polypeptide are known in the prior art and the skill of the artisan are well developed, knowledge regarding the redesign of up to 40% of a polypeptide molecule which would be able to fold and assume competent three dimensional structure capable of having the cholinesterase activity is lacking. Thus, searching for a polypeptide comprising a catalytic domain having 60%, 70%, 80% or 85% sequence homology to SEQ ID NO: 1 is well outside the realm of routine experimentation, and predictability of success in the art is extremely low. The amount of experimentation to identify a variant polypeptide comprising a polypeptide having up to 40% amino acid variation from those of SEQ ID NO:1 from any biological or man-made source is enormous. Since routine experimentation in the art does not include screening vast numbers of genomic, cDNA or man-made nucleic acid libraries, identifying the coding regions of cholineesterases, where the expectation of obtaining the desired cholinesterase is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the particular insects producing such a cholinesterase, and a general method to reengineer 40% of the amino acid residue of a protein comprising SEQ ID NO:1, and the amino acid residues which can be inserted, deleted or substituted without affecting the biological and/or chemical activity of the cholinesterase. Without such guidance, the experimentation left to those skilled in the art is undue.

Claims 1-3, 5, and 7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to all possible insect cholinesterase which comprises an amino acid sequence 60% identical or homologues to SEQ ID NO:1. The specification, however, only provides SEQ ID NO: 3, 5, and 126 comprising SEQ ID NO: 1 and SEQ ID NO: 7, 57 and 122 comprising an amino acid sequences having 94.3%, 94.1 and 99.8% identical to SEQ ID NO:1 encompassed by these claims.

The court of Appeals for the Federal Circuit has held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] name chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." UC California v. Eli Lilly (43 USPQ2d 1398). For claims drawn to genus, MPEP section 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Also, MPEP section 2163 states that a representative number of species mean that the species, which are adequately described, are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. At the time of invention, polypeptides comprising SEQ ID NO:1 having acetylcholinesterase were not known and the application discloses only several species comprising anamino acid sequence >94% identical to SEQ ID NO:1. Thus, the specification fails to describe additional representative species of these insect acetycholinesterase by any identifying structural characteristics or properties other than that they contain catalytic region >94% identical to SEQ ID NO: 1, for which no predictability of function is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, and 7 are rejected under 35 U.S.C. 102(a) as being anticipated by Weil *et al.* (IDS Reference: Proc. R. Soc. Lond. 13 (2002) 269, 2007-2016).

Weil *et al.* teach the amino acid sequence of cholinesterase (Ace1) from *Anapheles gambiae* which comprise the amino acid sequence of SEQ ID NO:1 (claims 1-3, 5, and 7). See Figur 1.

Applicants claiming foreign priority to 02/07622 filed 6/20/02 and 02/13799 filed 11/5/02 which filed in France is acknowledge. Applicant may overcome the above rejections by filing English translation of the foreign documents.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 5, and 7 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Bourguet *et al.* (Bourguet A, IDS Reference: J. Neurochemistry 1996, 67 (5), 2115-2123).

Claims 1-3, 5, and 7 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Bourguet *et al.* (Bourguet B, IDS Reference: Biochemical Genetics 1996, Vol 34, 351-362).

Bourguet A teach the isolation, purification and characterization of two acetylcholinesterase from *Cluex piplens mosquitol.* The first named AChE1 is sensitive to the carbamate insecticide propoxur, whereas the other is insensitive to inhibition by the insecticide. The exposure of insects to a concentration sufficient to inhibit AChE1 resulted ti the killing of all insects indicating that AChE1 fulfils the physiological function of neurotransmitter hydrolysis at the synapses. See abastract.

Bourguet B teach the purification and characterization of two forms of the AChE1 acetylcholinesterase from *Cluex piplens mosquitol.* In homozygous herbicide resistant mosquito strains from the Caribbean, herbicide resistant AChE1 is exclusively found. See abstract.

It appears that the purified AChE1 purified from *Cluex piplens mosquitol* Bourguet A and the two allelic variant taught by Bourguet B are identical to the claimed acetylcholinesterase of the claims.

The rejection is being made under 35 U.S.C. § 102(a) and 35 U.S.C. § 103 because it is not possible for the Examiner to physically compare the claimed Ace1 from

the AChE1 taught by Bourguet A and Bourguet B. Applicant bears the burden of providing evidence which distinguishes the claimed enzyme from that disclosed by Bourguet A and Bourguet B. A preferred means of providing this evidence is for applicant to submit a side-by-side comparison between the enzyme of the prior art and the claimed enzyme which demonstrates any material differences and shows the claimed Ace to be distinct and unobvious in view of the AChE1 of the prior art. *In re Best,* 430 USPQ (CCPA 1977) and *In re Fitzgerald,* 205 USPQ (CCPA 1980).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NASHAAT T. NASHED whose telephone number is (571)272-0934. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nashaat T. Nashed/
Primary Examiner, Art Unit 1656